(FILE 'HOME' ENTERED AT 11:09:22 ON 16 JAN 2004)

FILE 'MEDLINE, CANCERLIT, BIOSIS, EMBASE, CAPLUS' ENTERED AT 11:09:37 ON 16 JAN 2004

L1	530909	S	ENHANCER OR PROMOTER
L2	5840	S	EBNA1 OR EBNA2 OR EBNA-1 OR EBNA-2
L3	1306	S	L1 AND L2
L4	6889834	S	ACTIVATED OR INDUC?
L5	534	S	L4 AND L3
L6	978842	S	VECTOR OR PLASMID OR ADENOVIR? OR RETROVIR?
L7	152	S	L6 AND L5
L8	62		DUP REM L7 (90 DUPLICATES REMOVED)
L9	163	S	BCR2
L10	28	S	L9 AND L2
L11	8		DUP REM L10 (20 DUPLICATES REMOVED)
L12	7274	S	PAPILLOMA VIRUS AND E#
L13	887	S	L12 AND L1
L14	356	S	L13 AND L4
L15	136	S	L14 AND L6
L16	85		DUP REM L15 (51 DUPLICATES REMOVED)

L8 ANSWER 62 OF 62 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:536156 CAPLUS
DN 103:136156
TI A putative origin of replication of plasmids derived from Epstein-Barr virus is composed of two cis-acting components
AU Reisman, David; Yates, John; Sugden, Bill
CS McArdle Lab., Univ. Wisconsin, Madison, WI, 53706, USA
SO Molecular and Cellular Biology (1985), 5(8), 1822-32
CODEN: MCEBD4; ISSN: 0270-7306
DT Journal
LA English
AB A genetic element of Epstein-Barr virus, oriP, when present on recombinant plasmids, allowed the plasmids to replicate and to be maintained in cells that express the Epstein-Barr virus-encoded nuclear antigen **EBNA -1**. The DNA sequences required for oriP activity are described. Two noncontiguous regions of oriP were required in cis for activity. One consisted of .apprx.20 tandem, imperfect copies of a 30-base-pair (bp) sequence. The other required region, .apprx.1000 bp away, was .ltoreq.114 bp and contained a 65-bp region of dyad symmetry. When present together on a **plasmid**, these 2 components supported **plasmid** replication, even when the distance between them was varied and(or) their relative orientation was altered. When present alone on a **plasmid** that expresses a selectable marker, the family of 30-bp repeats efficiently conferred a transient drug-resistant phenotype on human 143 cells that was dependent on the **EBNA-1**. Apparently, **EBNA-1** interacts with the 30-bp repeated sequence to activate oriP. An SV40 virus early **promoter**, located in **plasmid** pA10CAT2, was **activated** by the 30-bp repeats in Raji cells (an EBNA-pos. Burkitt's lymphoma cell line) but not in EBNA-pos. 143 cells in which oriP also functions.

L8 ANSWER 61 OF 62 MEDLINE on STN DUPLICATE 25
AN 86284611 MEDLINE
DN 86284611 PubMed ID: 3016506
TI Mapping genetic elements of Epstein-Barr virus that facilitate extrachromosomal persistence of Epstein-Barr virus-derived plasmids in human cells.
AU Lupton S; Levine A J
SO MOLECULAR AND CELLULAR BIOLOGY, (1985 Oct) 5 (10) 2533-42.
Journal code: 8109087. ISSN: 0270-7306.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198609
ED Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860922
AB The Epstein-Barr virus (EBV) genome becomes established as a multicopy **plasmid** in the nucleus of infected B lymphocytes. A cis-acting DNA sequence previously described within the BamHI-C fragment of the EBV genome (J. Yates, N. Warren, D. Reisman, and B. Sugden, Proc. Natl. Acad. Sci. USA 81:3806-3810, 1984) allows stable extrachromosomal **plasmid** maintenance in latently infected cells, but not in EBV-negative cells. In agreement with the findings of Yates et al., deletion analysis permitted the assignment of this function to a 2,208-base-pair region (nucleotides 7315 to 9517 of the B95-8 strain of EBV) of the BamHI-C fragment that contained a striking repetitive sequence and an extended region of dyad symmetry. A recombinant **vector**, p410+, was constructed which carried the BamHI-K fragment (nucleotides 107565 to 112625 of the B95-8 strain, encoding the EBV-associated nuclear antigen **EBNA-1**), the cis-acting sequence from the BamHI-C fragment, and a dominant selectable marker gene encoding G-418 resistance in animal cells. After being transfected into HeLa cells, this **plasmid** persisted extrachromosomally at a low copy number, with no detectable rearrangements or deletions. Two mutations in the BamHI-K-derived portion of p410+, a large in-frame deletion and a linker insertion frameshift mutation, both of which alter the carboxy-terminal portion of **EBNA-1**, destroyed the ability of the **plasmid** to persist extrachromosomally in HeLa cells. A small in-frame deletion and linker insertion mutation in the region encoding the carboxy-terminal portion of **EBNA-1**, which replaced 19 amino acid codons with 2, had no effect on the maintenance of p410+ in HeLa cells. These observations indicate that **EBNA-1**, in combination with a cis-acting sequence in the BamHI-C fragment, is in part responsible for extrachromosomal EBV-derived **plasmid** maintenance in HeLa cells. Two additional activities have been localized to the BamHI-C DNA fragment: (i) a DNA sequence that could functionally substitute for the simian virus 40 **enhancer** and **promoter** elements controlling the expression of G-418 resistance and (ii) a DNA sequence which, although not sufficient to allow extrachromosomal **plasmid** maintenance, enhanced the frequency of transformation to G-418 resistance in EBV-positive (but not EBV-negative) cells. These findings suggest that the BamHI-C fragment contains a lymphoid-specific or EBV-**inducible promoter** or **enhancer** element or both.

L8 ANSWER 58 OF 62 CANCERLIT on STN
AN 87638190 CANCERLIT
DN 87638190
TI ELEMENTS REQUIRED FOR REPLICATION AND MAINTENANCE OF THE EPSTEIN-BARR VIRAL GENOME.
AU Reisman D J
CS Univ. of Wisconsin, Madison, WI.
SO Diss Abstr Int (Sci), (1986) 47 (3) 937.
ISSN: 0419-4217.
DT (THESIS)
LA English
FS Institute for Cell and Developmental Biology
EM 198711
ED Entered STN: 19941107
Last Updated on STN: 19941107
AB Epstein-Barr virus (EBV) is a human herpesvirus that infects B-lymphocytes both in vivo and in vitro and transforms them into proliferating B-lymphoblasts. The viral genome is present in transformed cells in multiple copies as a supercoiled DNA **plasmid** of approximately 172,000 base pairs. The experiments presented in this thesis describe some of the requirements for the establishment and maintenance of the viral genome in the transformed cell. In one series of experiments, EBV-genome-negative B-lymphoid cell lines were infected with EBV (B95-8 strain). The infections were abortive as monitored by **induction** of a series of nuclear antigens (EBNAs). One cell line, originally thought to be derived from the EBV-genome-negative line, Ramos, expressed levels of EBNA that were undetectable by anti-complement immunofluorescence, but was shown to express **EBNA-1** by its ability to support the replication of recombinant plasmids that carry oriP (see below). However, this cell line was found to contain 1-2 copies of the EBV genome (P3HR-1 strain) and was designated TG8. Superinfection of this cell line by B95-8 EBV led to the expression of EBNA, and both circularization and limited replication of the superinfecting genome. The infection was abortive and the superinfecting viral DNA was selectively eliminated from the population. A second series of experiments was performed to define the sequences required for the activity of a putative EBV origin of DNA replication, oriP. When present in cis, oriP permits replication of plasmids in EBV-genome-positive cells or in cells that express **EBNA-1**. Two non-contiguous components of oriP are required for **plasmid** replication: a 20-member family of tandem 30-base pair (bp) direct repeats and a sequence containing a 65-bp dyad symmetry element. In addition to its being required for **plasmid** replication, the 20-member family of repeats has activity as a transcriptional **enhancer** that is **activated** in trans, presumably upon binding with the **EBNA-1** protein. The 30-bp family of repeats enhances expression of the chloramphenicol acetyl transferase gene expressed from either the SV40 early **promoter** or the herpes simplex thymidine kinase **promoter**. Transcriptional enhancement requires the expression of the **EBNA-1** gene.

L8 ANSWER 52 OF 62 MEDLINE on STN DUPLICATE 21
AN 89259046 MEDLINE
DN 89259046 PubMed ID: 2542579
TI Multiple **EBNA1**-binding sites are required to form an **EBNA1**-dependent **enhancer** and to activate a minimal replicative origin within oriP of Epstein-Barr virus.
AU Wysokenski D A; Yates J L
CS Department of Human Genetics, Roswell Park Memorial Institute, Buffalo, New York 14263.
SO JOURNAL OF VIROLOGY, (1989 Jun) 63 (6) 2657-66.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198906
ED Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890627
AB **EBNA1** activates the EBV **plasmid** maintenance sequence oriP by binding to its two essential regions. One region is a family of 30-base-pair (bp) repeats and is **activated** by **EBNA1** to act as a transcriptional **enhancer**. The other region contains a 65-bp dyad symmetry and lacks **enhancer** function. To explore the functional differences between the two regions, we determined oriP activities as functions of the number of 30-bp repeats and compared them with activities determined when tandem copies of the dyad symmetry region were used to replace the 30-bp repeats. Three conclusions have been drawn. (i) Activation of the 30-bp repeats by **EBNA1** to enhance transcription or to permit **plasmid** maintenance is a highly cooperative process involving at least six or seven 30-bp repeats for full activity. (ii) Tandem copies of the dyad symmetry region cooperatively enhance transcription but are less effective than 30-bp repeats providing a similar number of **EBNA1**-binding sites. (iii) Tandem copies of the dyad symmetry region alone cooperatively activate replication, suggesting that the region contains the actual origin of replication. We also report that while rodent-derived cell lines do not support replication of EBV-derived plasmids they do permit **EBNA1**-dependent **enhancer** activity. EBV **plasmid** replication thus requires the interaction of **EBNA1** or oriP with a host factor that is not required for enhancement of transcription.

L8 ANSWER 50 OF 62 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 20
AN 1990:292992 BIOSIS
DN PREV199090023838; BA90:23838
TI EPSTEIN-BARR VIRUS LATENT MEMBRANE PROTEIN LMP1 AND NUCLEAR PROTEINS 2 AND 3C ARE EFFECTORS OF PHENOTYPIC CHANGES IN B LYMPHOCYTES **EBNA-2** AND LMP1 COOPERATIVELY **INDUCE** CD23.
AU WANG F [Reprint author]; GREGORY C; SAMPLE C; ROWE M; LIEBOWITZ D; MURRAY R; RICKINSON A; KIEFF E
CS DEP MED, HARVARD MED SCH, 75 FRANCIS ST, BOSTON, MASS 02115, USA
SO Journal of Virology, (1990) Vol. 64, No. 5, pp. 2309-2318.
CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 23 Jun 1990
Last Updated on STN: 23 Jun 1990
AB Latent Epstein-Barr virus (EBV) infection and growth transformation of B lymphocytes is characterized by EBV nuclear and membrane protein expression (EBV nuclear antigen [EBNA] and latent membrane protein [LMP], respectively). LMP1 is known to be an oncogene in rodent fibroblasts and to **induce** B-lymphocyte activation and cellular adhesion molecules in the EBV-negative Burkitt's lymphoma cell line Louckes. **EBNA-2** is required for EBV-**induced** growth transformation; it lowers rodent fibroblast serum dependence and specifically **induces** the B-lymphocyte activation antigen CD23 in Louckes cells. These initial observations are now extent through an expanded study of EBNA- and LMP1-**induced** phenotypic effects in a different EBV-negative B-lymphoma cell line, BJAB. LMP1 effects were also evaluated in the EBV-negative B-lymphoma cell line BL41 and the EBV-positive Burkitt's lymphoma cell line. Daudi (Daudi is deleted for **EBNA-2** and does not express LMP). Previously described **EBNA-2**- and LMP1-transfected Louckes cells were studied in parallel. **EBNA-2**, from EBV-1 strains but not EBV-2, **induced** CD23 and CD21 expression in transfected BJAB cells. In contrast, EBNA-3C **induced** CD21 but not CD23, while no changes were evident in **vector** control-, **EBNA-1**-, or EBNA-LP-transfected clones. EBNAs did not affect CD10, CD30, CD39, CD40, CD44, or cellular adhesion molecules. LMP1 expression in all cell lines **induced** growth in large clumps and expression of the cellular adhesion molecules ICAM-1, LFA-1, and LFA-3 in those cell lines which constitutively express low levels. LMP1 expression **induced** marked homotypic adhesion in the BJAB cell line, despite the fact that there was no significant increase in the high constitutive BJAB LFA-1 and ICAM-1 levels, suggesting that LMP1 also **induces** an associated functional change in these molecules. LMP1 **induction** of these cellular adhesion molecules was also associated with increased heterotypic adhesion to T lymphocytes. The Burkitt's lymphoma marker, CALLA (CD10), was uniformly down regulated by LMP1 in all cell lines. In contrast, LMP1 **induced** unique profiles of B-lymphoma activation antigens in the various cell lines. LMP1 **induced** CD23 and CD39 in BJAB; CD23 in Louckes; CD39 and CD40 in BL41; and CD21, CD40, and CD44 in Daudi. In BJAB, CD23 surface and mRNA expression were markedly increased by **EBNA-2** and LMP1 coexpression, compared with **EBNA-2** or LMP1 alone. This cooperative effect was CD23 specific, since no such effect was observed on another marker, CD21. S1 analyses revealed that BJAB cells express low levels of Fc.epsilon.RIIa CD23 mRNA, and Fc.epsilon.RIIb CD23 mRNA was not detectable. LMP1 preferentially increases Fc.epsilon.RIIb CD23 mRNA. **EBNA-2** expression alone in BJAB increases the constitutively expressed Fc.epsilon.RIIa CD23 mRNA. However, when coexpressed with LMP1, **EBNA-2** increases total CD23 mRNA without altering the high relative abundance of Fc.epsilon.RIIb to

Fc.epsilon.RIIa CD23 mRNA **induced** by LMP1. Thus, LMP1 likely activates the Fc.epsilon.RIIb CD23 **promoter**, while **EBNA -2** more likely transactivates a regulatory element common to both the Fc.epsilon.RIIa and Fc.epsilon.RIIb promoters.

L8 ANSWER 47 OF 62 MEDLINE on STN DUPLICATE 18
AN 92015480 MEDLINE
DN 92015480 PubMed ID: 1656076
TI An Epstein-Barr virus nuclear protein 2 domain essential for transformation is a direct transcriptional activator.
AU Cohen J I; Kieff E
CS Medical Virology Section, National Institutes of Health, Bethesda, Maryland 20892.
NC CA47006 (NCI)
SO JOURNAL OF VIROLOGY, (1991 Nov) 65 (11) 5880-5.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199111
ED Entered STN: 19920124
Last Updated on STN: 19980206
Entered Medline: 19911114
AB Epstein-Barr virus nuclear protein 2 (**EBNA-2**) increases mRNA levels of specific viral and cellular genes through direct or indirect effects on upstream regulatory elements. The **EBNA-2** domains essential for these effects have been partially defined and correlate with domains important for B-cell growth transformation. To determine whether **EBNA-2** has a direct transcriptional activating domain, gene fusions between the DNA-binding domain of GAL4 and **EBNA-2** were tested in CHO and B-lymphoma cells for the ability to activate transcription from target plasmids containing GAL4 recognition sites upstream of an **adenovirus** or murine mammary tumor virus **promoter**. In B-lymphoma cells, a 37-amino-acid **EBNA-2** domain previously identified to be essential for transformation was nearly as strong a transcriptional activator as the activating domain of herpes simplex virus trans-**inducing** factor VP16. A quadradecapeptide had about 25% of the activating activity of the longer peptide. This first evidence that **EBNA-2** directly activates transcription should facilitate the identification of nuclear factors with which **EBNA-2** interacts in transactivation and transformation.

L8 ANSWER 46 OF 62 MEDLINE on STN DUPLICATE 17
AN 92046339 MEDLINE
DN 92046339 PubMed ID: 1658373
TI Delineation of the cis-acting element mediating **EBNA-2** transactivation of latent infection membrane protein expression.
AU Tsang S F; Wang F; Izumi K M; Kieff E
CS Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115.
NC CA01395 (NCI)
CA47006 (NCI)
CA52244 (NCI)
+
SO JOURNAL OF VIROLOGY, (1991 Dec) 65 (12) 6765-71.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199112
ED Entered STN: 19920124
Last Updated on STN: 19980206
Entered Medline: 19911226
AB To delineate the cis-acting element through which **EBNA-2** transactivates latent membrane protein 1 (LMP1), we assayed the effect of **EBNA-2** on the activity of LMP1 **promoter** upstream deletion mutants in the context of the LMP1 or heterologous promoters controlling chloramphenicol acetyltransferase (CAT) reporter gene expression in Epstein-Barr virus-negative Burkitt lymphoma cells. Assays of progressive 5' deletions of the LMP1 **promoter** revealed low constitutive and at least eightfold **EBNA-2** -stimulated activity from -512 to +40 (-512/+40), -334/+40, and -234/+40 LMP1CAT plasmids. More extensive 5'-deleted -205/+40, -155/+40, and -147/+40 LMP1CAT plasmids also had low constitutive activity but were not **EBNA-2** responsive. The most 5'-deleted -55/+40 LMP1CAT **plasmid** had moderate constitutive activity and was not **EBNA-2 inducible**. Either orientation of the -334/+40 LMP1 sequence conferred **EBNA-2** responsiveness when positioned upstream of an enhancerless simian virus 40 or herpes simplex virus thymidine kinase (TK) **promoter**. **EBNA-2** and the cis-acting LMP1 DNA were both required to increase TK **promoter**-initiated mRNA, indicating that the **EBNA-2** effect is at the transcriptional level. Further deletion analysis of the **EBNA-2**-responsive cis-acting element defined a -234/-92 LMP1 DNA fragment which conveyed **EBNA-2** responsiveness to the herpes simplex virus TK **promoter**. The 5' 30 bp between -234 and -205 were essential for **EBNA-2** responsiveness. Thus, these experiments define a 142-bp cis-acting element which is sufficient for conveying **EBNA-2** responsiveness and an essential 30-bp component of that element. The role of this element in LMP1 and LMP2B expression and its possible role in LMP2A expression are discussed.

L8 ANSWER 43 OF 62 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:647988 CAPLUS
Correction of: 1994:479757
DN 121:247988
Correction of: 121:79757
TI **EBNA2** activation of transcription via E2 factor binding sites requires E2F and Rb protein
AU Sample, Clare; Hiebert, Scott; Kieff, Elliott
CS Dep. Virol. Mol. Biol. Tumor Coll. Biol., St. Jude Child. Res. Hosp., Memphis, TN, 38105, USA
SO Colloque INSERM (1993), 225(Epstein-Barr Virus and Associated Diseases), 165-8
CODEN: CINMDE; ISSN: 0768-3154
DT Journal
LA English
AB The mechanism of **EBNA2** activation of target promoters was studied. Epstein-Barr virus-neg. B cells were cotransfected with target **promoter**-CAT constructs and plasmids expressing a gene for **EBNA2** or **EBNA2** lacking a putative Rb binding domain. The target **promoter** consisted of 85 bp of the **adenovirus** E2 **promoter**. **EBNA2 activated** the E2-CAT constructs in a manner consistent with activation of the E2F transcription factor. Activation required the putative Rb binding domain.

L8 ANSWER 42 OF 62 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:10466 CAPLUS
DN 122:25166
TI Delineation of the cis-acting sequence mediating transactivation of a bi-directional latent **promoter** region by Epstein-Barr virus nuclear antigen 2 (**EBNA2**)
AU Laux, Gerhard; Dugrillon, Frank; Eckert, Christine; Zimber-Strobl, Ursula; Bornkamm, Georg W.
CS Inst. Klin. Molekularbiol. Tumorgenet., GSF-Forschungszent. Umwelt Gesundheit, GmbH, Muenchen, D-8000/70, Germany
SO Colloque INSERM (1993), 225(Epstein-Barr Virus and Associated Diseases), 211-17
CODEN: CINMDE; ISSN: 0768-3154
DT Journal
LA English
AB The authors assayed the effect of **EBNA2** on the activity of a bi-directional latent **promoter** region, driving transcription of terminal protein 2 (TP2) and latent membrane protein (LMP) genes in opposite directions. Gene expression of upstream deletion mutants of TP2 and LMP **promoter** luciferase (LUC) reporter constructs was tested after cotransfection with an **EBNA2** expression **vector** in BL41.cntdot.P3HR1 cells, which do not express **EBNA2**. Progressive 5' deletions of the TP2 **promoter** revealed .gtoreq.28-fold **EBNA2 induced** activity from -276 to +91 and -104 to +91 TP2LUC plasmids. More extended 5' deletions of the TP2 **promoter** (-84 to +91 and -64 to +91) were not **EBNA2** responsive anymore. Progressive 5' deletions of the LMP **promoter** revealed .gtoreq.25-fold **EBNA2** stimulated activity from -327 to +40 and -232 to +40. More extended 5' deletions of the LMP **promoter** (-199 to +40, -154 to +40, -132 to +40, -79 to +40, and -34 to +40) were not **EBNA2** responsive anymore. Thus, these assays defined a 195 bp and a 232 bp cis-acting sequence element which is sufficient for conveying **EBNA2** transactivation of the TP2 and LMP **promoter**, resp. Both sequences overlap by 100 bp which transferred stimulation by **EBNA2** to a heterologous minimal .beta.-globin **promoter** controlling LUC reporter gene expression. Sequences of 20 bp and 33 bp located at both ends of the 100 bp element seem to be essential for transactivation by **EBNA2**.

L8 ANSWER 41 OF 62 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 1993:273897 BIOSIS
DN PREV199396004122
TI Epstein-Barr virus nuclear antigen 2 transactivates the long terminal repeat of human immunodeficiency virus type 1.
AU Scala, Giuseppe [Reprint author]; Quinto, Ileana; Ruocco, Maria R.; Mallardo, Massimo; Ambrosino, Concetta; Squitieri, Battista; Tassone, Pierfrancesco; Venuta, Salvatore
CS Dipartimento di Biochimica e Biotecnologie Mediche, Universita Federico II, 80131 Naples, Italy
SO Journal of Virology, (1993) Vol. 67, No. 5, pp. 2853-2861.
CODEN: JOVIAM. ISSN: 0022-538X.
DT Article
LA English
ED Entered STN: 9 Jun 1993
Last Updated on STN: 9 Jun 1993
AB Human immunodeficiency virus type 1 (HIV-1)-infected subjects show a high incidence of Epstein-Barr virus (EBV) infection. This suggests that EBV may function as a cofactor that affects HIV-1 activation and may play a major role in the progression of AIDS. To test this hypothesis, we generated two EBV-negative human B-cell lines that stably express the **EBNA2** gene of EBV. These **EBNA2**-positive cell lines were transiently transfected with plasmids that carry either the wild type or deletion mutants of the HIV-1 long terminal repeat (LTR) fused to the chloramphenicol acetyltransferase (CAT) gene. There was a consistently higher HIV-1 LTR activation in **EBNA2**-expressing cells than in control cells, which suggested that **EBNA2** proteins could activate the HIV-1 **promoter**, possibly by **inducing** nuclear factors binding to HIV-1 cis-regulatory sequences. To test this possibility, we used CAT-based plasmids carrying deletions of the NF-kappa-B (pNFA-CAT), Sp1 (pSpA-CAT), or TAR (pTAR-CAT) region of the HIV-1 LTR and retardation assays in which nuclear proteins from **EBNA2**-expressing cells were challenged with oligonucleotides encompassing the NF-kappa-B or Sp1 region of the HIV-1 LTR. We found that both the NF-kappa-B and the Sp1 sites of the HIV-1 LTR are necessary for **EBNA2** transactivation and that increased expression resulted from the **induction** of NF-kappa-B-like factors. Moreover, experiments with the TAR-deleted pTAR-CAT and with the tat-expressing pAR-TAT plasmids indicated that endogenous Tat-like proteins could participate in **EBNA2**-mediated activation of the HIV-1 LTR and that **EBNA2** proteins can synergize with the viral tat transactivator. Transfection experiments with plasmids expressing the **EBNA1**, EBNA3, and EBNALP genes did not cause a significant HIV-1 LTR activation. Thus, it appears that among the latent EBV genes tested, **EBNA2** was the only EBV gene active on the HIV-1 LTR. The transactivation function of **EBNA2** was also observed in the HeLa epithelial cell line, which suggests that EBV and HIV-1 infection of non-B cells may result in HIV-1 **promoter** activation. Therefore, a specific gene product of EBV, **EBNA2**, can transactivate HIV-1 and possibly contribute to the clinical progression of AIDS.

L8 ANSWER 36 OF 62 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95335827 EMBASE
DN 1995335827
TI Domains of the Epstein-Barr virus nuclear antigen 2 (**EBNA2**) involved in the transactivation of the latent membrane protein 1 and the EBNA Cp promoters.
AU Sjoblom A.; Nerstedt A.; Jansson A.; Rymo L.
CS Dept. Clin. Chem. Transfusion Med., Sahlgrenska University Hospital, Goteborg University,S-413 45 Gothenburg, Sweden
SO Journal of General Virology, (1995) 76/11 (2669-2678).
ISSN: 0022-1317 CODEN: JGVIAY
CY United Kingdom
DT Journal; Article
FS 004 Microbiology
022 Human Genetics
LA English
SL English
AB The Epstein-Barr virus (EBV) nuclear antigen 2 (**EBNA2**) is one of the first EBV-encoded gene products expressed after infection of primary B lymphocytes. **EBNA2** is essential for the growth-transforming potential of the virus and it functions as a transcriptional activator of a set of viral and cellular genes. Sequence-specific DNA-binding by **EBNA2** has not been demonstrated but the molecule is targeted to specific DNA regions by a cellular protein, RBP-J.kappa., which recognizes the GTGGGAA sequence present in the regulatory region of all **EBNA2** -responsive promoters defined so far. We have determined the contribution of a RBP-J.kappa. recognition sequence, an adjacent interferon-stimulated response element (ISRE) motif and a PU.1-binding site in the LMP1 regulatory sequence (LRS) to **EBNA2-induced** transactivation of the **promoter** by site-directed mutagenesis of LRS-carrying reporter plasmids. **EBNA2** responsiveness was reduced by approximately twofold when either or both of the RBP-J.kappa.-binding and ISRE sequences were mutated. ISRE seemed to function as an **EBNA2**-independent positive element. On the other hand, mutation of the PU box resulted in a drastic reduction of **EBNA2** responsiveness, irrespective of whether the RBP-J.kappa. site or the ISRE motif was present. A comparative study by deletion mutation identified regions of EBV B95-8 **EBNA2** involved in the transactivation of the LMP1 and the EBNA Cp promoters. Two domains of **EBNA2** defined by deletion of amino acids 247-337 and 437-476 were found to be important for the activation of both promoters, while two different domains corresponding to residues 4-18 and 118-198 were required solely for the LMP1 **promoter**. Thus, **EBNA2** must activate the LMP1 and Cp promoters by different mechanisms. All deletions involved in transcriptional activation of the two promoters contained regions that are conserved in **EBNA2** of B95-8 EBV (type 1), AG876 EBV (type 2) and herpesvirus papio origin.

L8 ANSWER 34 OF 62 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:761795 CAPLUS
DN 123:132861
TI **Adenovirus** expression vectors using tumor-**inducible** expression cassettes for gene therapy in cancers
IN Dedieu, Jean-Francois; Le, Roux Aude; Perricaudet, Michel
PA Rhone-Poulenc Rorer S.A., Fr.
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9514101	A1	19950526	WO 1994-FR1284	19941107
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2712602	A1	19950524	FR 1993-13766	19931118
	FR 2712602	B1	19960209		
	CA 2176585	AA	19950526	CA 1994-2176585	19941107
	AU 9481471	A1	19950606	AU 1994-81471	19941107
	AU 699867	B2	19981217		
	EP 729516	A1	19960904	EP 1995-900795	19941107
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09504955	T2	19970520	JP 1994-514247	19941107
	ZA 9409103	A	19950721	ZA 1994-9103	19941116
	US 5837531	A	19981117	US 1996-646246	19960513
	NO 9601977	A	19960514	NO 1996-1977	19960514
	FI 9602114	A	19960517	FI 1996-2114	19960517
PRAI	FR 1993-13766		19931118		
	WO 1994-FR1284		19941107		

AB Viral expression vectors with a therapeutic gene under the control of expression signals specifically active in tumor cells, and their prepn. and use in the treatment and prevention of cancers are described. The preferred virus is a replication-defective **adenovirus**. The gene may be a tumor suppressor gene, or it may encode a cytotoxin, a lymphokine, or a prodrug activating enzyme (such as a thymidine kinase). The **promoter** may be derived from an oncogenic virus. The construction of such vectors using a chimeric **promoter** derived from the Epstein-Barr nuclear antigen 1 and terminal protein 1 genes is demonstrated. **EBNA1**-dependent **induction** of reporter gene expression was demonstrated.

L8 ANSWER 27 OF 62 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:236032 CAPLUS
DN 129:3441
TI The expression of matrix metalloproteinase 9 is enhanced by Epstein-Barr virus latent membrane protein 1
AU Yoshizaki, Tomokazu; Sato, Hiroshi; Furukawa, Mitsuru; Pagano, Joseph S.
CS Department of Otolaryngology, School of Medicine, Cancer Research Institute, Kanazawa University, Ishikawa, 920, Japan
SO Proceedings of the National Academy of Sciences of the United States of America (1998), 95(7), 3621-3626
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Matrix metalloproteinases (MMPs) are frequently expressed in malignant tumor cells and are thought to play crucial roles in tumor invasion and metastasis. Here the authors report that expression of MMP9 is increased in Epstein-Barr virus (EBV)-infected type III latency lymphoma cell lines, but not in type I lines where latent viral gene expression is highly restricted. Type III cell lines express abundant EBV latent membrane protein 1 (LMP1), the principal EBV oncoprotein, as well as the other latency proteins including the transcriptional factor, EBV nuclear antigen 2, which is also required for cell immortalization. Transfection of an LMP1 expression **plasmid** in the C33A cell line increased MMP9 expression, whereas overexpression of EBV nuclear antigen 2 did not. Three motifs, homologous to the binding sites of NF-.kappa.B, SP-1, and AP-1 proteins, contribute to **induction** of the MMP9 **promoter** by 12-O-tetradecanoyl-phorbol-13-acetate and tumor necrosis factor .alpha.. Here the authors report that binding sites for NF-.kappa.B, SP-1, and AP-1 also contribute to **induction** of the MMP9 **promoter** by the viral protein, LMP1, mainly through the NF-.kappa.B and, to a lesser extent, the SP-1 and AP-1 sites. Moreover the AP-1 binding site is essential in that mutation of it abolished reporter gene **induction** by LMP1. The enhancement of MMP9 expression was blocked by cotransfection of an I.kappa.B expression **plasmid**. Thus in addn. to its transforming properties, the oncoprotein LMP1 may contribute to invasiveness and metastasis of EBV-assocd. tumors such as nasopharyngeal carcinoma.

11 ANSWER 8 OF 8 MEDLINE on STN DUPLICATE 5
AN 92141227 MEDLINE
DN 92141227 PubMed ID: 1371012
TI Host-cell-phenotype-dependent control of the **BCR2**/BWR1 promoter complex regulates the expression of Epstein-Barr virus nuclear antigens 2-6.
CM Erratum in: Proc Natl Acad Sci U S A 1992 Jul 1;89(13):6225
AU Altiok E; Minarovits J; Hu L F; Contreras-Brodin B; Klein G; Ernberg I
CS Department of Tumor Biology, Karolinska Institute, Stockholm, Sweden.
NC 1R01 CA 52225 (NCI)
2R01 CA 30264 (NCI)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Feb 1) 89 (3) 905-9.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199203
ED Entered STN: 19920329
Last Updated on STN: 19980206
Entered Medline: 19920310
AB Epstein-Barr virus nuclear antigens (EBNAs) are expressed in a cell-phenotype-dependent manner. **EBNA 1** is regularly expressed in all Epstein-Barr virus-carrying cells, whereas EBNAs 2-6 are only expressed in Epstein-Barr virus-carrying cells with a lymphoblastoid phenotype including group III Burkitt lymphoma (BL) lines positive for B-cell activation markers. Transcripts are initiated at the **BCR2** or exceptionally at one BWR1 promoter in lymphoblastoid cell lines and group III BL lines. In group I BL lines, nasopharyngeal carcinoma, and the somatic cell hybrids, where EBNAs 2-6 are downregulated, the **BCR2**/BWR1 promoter complex is inactive or switched off. Upregulation of EBNAs 2-6 in group III BL cells and in 5-azacytidine-treated group I BL cells accompanies the activation of the silent **BCR2**/BWR1 promoters. Activation of **BCR2** parallels demethylation of at least one CpG pair in the same promoter region. The activity of **BCR2**/BWR1 promoter complex depends on a particular B-cell phenotype. **EBNA 1** transcription must be initiated at another promoter in cells that express only **EBNA 1**.

L11 ANSWER 5 OF 8 MEDLINE on STN DUPLICATE 3
AN 93212510 MEDLINE
DN 93212510 PubMed ID: 8384755
TI Viral and cellular factors influence the activity of the Epstein-Barr virus **BCR2** and BWR1 promoters in cells of different phenotype.
AU Nilsson T; Sjoblom A; Masucci M G; Rymo L
CS Department of Clinical Chemistry, University of Goteborg, Sahlgren's Hospital, Gothenburg, Sweden.
NC 1R01 CA 52225 (NCI)
SO VIROLOGY, (1993 Apr) 193 (2) 774-85.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199304
ED Entered STN: 19930514
Last Updated on STN: 19970203
Entered Medline: 19930423
AB Transformation of B-lymphocytes by Epstein-Barr virus (EBV) is characterized by the expression of six viral nuclear antigens (**EBNA1** to EBNA6) which are encoded by messages derived from long primary transcripts initiated at one of two promoters located in the BamHI C (**BCR2**) and BamHI W (BWR1) regions of the viral genome. The BWR1 promoter is preferentially utilized during the initial phases of EBV infection, whereas the **BCR2** promoter is almost invariably used in transformed lymphoblastoid cell lines (LCLs). In order to gain some insight into the molecular mechanisms underlying promoter usage we have analyzed the activity of reporter plasmids carrying different parts of the BWR1 and **BCR2** regulatory sequences in EBV-negative and EBV-carrying B cell lines that, on the basis of their surface marker expression, are representative of different stages of B cell activation/differentiation. We show that: (i) there is an inverse correlation between the activity of BWR1 and oriP-containing **BCR2** reporter plasmids in cell lines expressing a BL group I versus a group III phenotype, the BWR1 promoter being virtually inactive in group III cells; (ii) **BCR2** reporter plasmids devoid of the oriP region are active in EBV-negative cell lines and EBV-positive cells expressing a group I or group II phenotype and virtually inactive in BL group III cells and LCLs, suggesting that cellular factors are required for activation of **BCR2** promoter elements. These factors are lost upon progression to a group III phenotype); (iii) expression of **EBNA2** is sufficient to activate reporter plasmids containing the proximal part of the **BCR2** promoter in EBV negative cells, whereas coexpression of **EBNA2** and **EBNA1** is required to activate the promoter in oriP-containing plasmids; (iv) the 30-bp repeat region of oriP acts as a negative cis-element on downstream promoters but is transformed into a transcriptional enhancer by the concerted action of **EBNA1** and cellular factors. There was a poor correlation between the activity of exogenous reporter plasmids and endogenous BWR1 and **BCR2** promoters in phenotypically different EBV-positive cell lines. The presence of the appropriate trans-acting factors was not sufficient to activate the endogenous BWR1 and **BCR2** promoters in BL cells expressing a group I phenotype.

L11 ANSWER 2 OF 8 MEDLINE on STN DUPLICATE 2
AN 96211488 MEDLINE
DN 96211488 PubMed ID: 8648690
TI Transcription of the Epstein-Barr virus nuclear antigen 1 (**EBNA1**) gene occurs before induction of the **BCR2** (Cp) EBNA gene promoter during the initial stages of infection in B cells.
AU Schlager S; Speck S H; Woisetschlager M
CS Sandoz Forschungsinstitut, Vienna, Austria.
NC R01 CA43143 (NCI)
SO JOURNAL OF VIROLOGY, (1996 Jun) 70 (6) 3561-70.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199607
ED Entered STN: 19960805
Last Updated on STN: 19960805
Entered Medline: 19960723
AB The purpose of this study was to gain insights into the regulation of Epstein-Barr virus (EBV) gene transcription during the establishment of viral latency in B cells. During the early stages of EBV infection in B lymphocytes, transcription of six viral nuclear antigens (EBNAs) is initiated from an early promoter (Wp). This is followed by a switch of promoter usage to an upstream promoter, Cp, whose activity is autoregulated by both **EBNA1** and **EBNA2**. Previously it was demonstrated that infection of primary B cells with **EBNA2**-negative (**EBNA2**-) EBNA4-mutant (EBNA4mut) virus resulted only in the expression of mutant EBNA4 protein and failure to express the other EBNA gene products (C. Rooney H. G. Howe, S. H. Speck, and G. Miller, J. Virol. 63:1531-1539, 1989). We extended this research to demonstrate that Wp-to-Cp switching did not occur upon infection of primary B cells with an **EBNA2**- EBNA4mut virus (M. Woisetschlaeger, X. W. Jin, C. N. Yandara, L. A. Furmanski, J. L. Strominger, and S. H. Speck, Proc. Natl. Acad. Sci. USA 88:3942-3946, 1991). Further characterization of this phenomenon led to the identification of an **EBNA2**-dependent enhancer upstream of Cp. On the basis of these data, a model was proposed in which initial transcription from Wp gives rise to the expression of **EBNA2** and EBNA4, and then transcription is upregulated from Cp via the **EBNA2**-dependent enhancer (Woisetschlaeger et al., as noted above). Implicit in this model is that transcription of the **EBNA1** and EBNA3a to -3c genes is dependent on the switch from Wp to Cp, since primary cells infected with **EBNA2**- EBNA4mut virus fail to switch and also fail to express these viral antigens. Here we critically evaluate this model and demonstrate, in contrast to the predictions of the model, that transcription of both the **EBNA1** and **EBNA2** genes precedes activation of Cp. Furthermore, the level of **EBNA1** gene transcription was strongly reduced in primary B cells infected with **EBNA2**- EBNA4mut virus compared with that of cells infected with wild-type virus. Switching to Cp, as well as **EBNA1** gene transcription, was observed upon infection of EBV-negative Burkitt's lymphoma (BL) cell lines with **EBNA2**- EBNA4mut virus, thus establishing a correlation between early **EBNA1** gene transcription and upregulation of transcription initiation from Cp. However, in EBV-negative BL cell lines infected with **EBNA2**-EBNA4mut virus, transcription of the **EBNA1** gene at early time points postinfection initiated from Qp, the **EBNA1** gene promoter active in group I BL cells (B. C. Schaefer, J. L. Strominger, and S. H. Speck, Proc. Natl. Acad. Sci. USA 92:10565-10569, 1995), rather than from Wp. The data support a model in which **EBNA1** plays an important role in the cascade of events leading to successful switching from Wp to Cp and subsequent immortalization of the infected B cell.

L16 ANSWER 79 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:1316 CAPLUS
DN 108:1316
TI RNA probes to analyze human papillomavirus gene expression in squamous papilloma of the respiratory tract
AU Ward, P.; Wu, T. C.; Mounts, P.
CS Sch. Public Health, Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO Cancer Cells (1984-1989) (1987), 5(Papillomaviruses), 73-8
CODEN: CACEEG; ISSN: 0743-2194
DT Journal
LA English
AB Viral gene expression in human papillomavirus type 6 (HPV-6)-**induced** respiratory tract lesions was studied. To facilitate the prodn. in vitro of strand-specific RNA probes, recombinant plasmids between subgenomic fragments of HPV-6e and **plasmid** pGEM-1 were made. Plasmids were constructed by inserting the 2400-bp and 5600-bp BamHI-HindIII subgenomic fragments of HPV-6e into the **vector**. This construction allows the prodn. of both sense and antisense RNA probes by transcription from either the Sp6 or the T7 **promoter** of pGEM-1. Using these riboprobes, an RNA of 1200 nucleotides was identified in RNA extd. from respiratory papillomata **induced** by HPV-6e. On the basis of size and genomic location, it is speculated that this RNA may correspond to the product of the putative **E2** open reading frame.

L16 ANSWER 63 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:588468 CAPLUS
DN 111:188468
TI The **E6** and **E7** genes of the human papillomavirus type 16 together are necessary and sufficient for transformation of primary human keratinocytes
AU Muenger, Karl; Phelps, William C.; Bubb, Vivien; Howley, Peter M.; Schlegel, Richard
CS Lab. Tumor Virus Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Journal of Virology (1989), 63(10), 4417-21
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB The early human papillomavirus type 16 genes that directly participate in the in vitro transformation of primary human keratinocytes have been defined. In the context of the full viral genome, mutations in ether the **E6** or **E7** open reading frame completely abrogated transformation of these cells. Mutations in the **E1**, **E2**, and **E2**-**E4** open reading frames, on the other hand, had no effect. Thus, both the full-length **E6** and **E7** genes were required for the **induction** of keratinocyte immortalization and resistance to terminal differentiation. The **E6** and **E7** genes expressed together from the human .beta.-actin **promoter** were sufficient for this transformation; mutation of either gene in the context of this recombinant **plasmid** eliminated the ability to **induce** stable differentiation-resistant transformants.

L16 ANSWER 52 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:576231 CAPLUS
DN 115:176231
TI The full-length **E6** protein of human papillomavirus type 16 has transforming and trans-activating activities and cooperates with **E7** to immortalize keratinocytes in culture
AU Sedman, Sylvia A.; Barbosa, Miguel S.; Vass, William C.; Hubbert, Nancy L.; Haas, Jonathan A.; Lowy, Douglas R.; Schiller, John T.
CS Lab. Cell. Oncol., Natl. Cancer Inst., Bethesda, MD, 20892, USA
SO Journal of Virology (1991), 65(9), 4860-6
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB The wild-type **E6** and **E7** genes of human papillomavirus type 16 (HPV16) can cooperate to immortalize normal human keratinocytes in culture. The **E6** open reading frame of HPV16 and other HPV types highly assocd. with cervical cancer has the potential of encoding both full-length **E6** and two truncated **E6** proteins, the latter being generated via splicing within the **E6** open frame portion of the **E6**-**E7** polycistronic transcript. Those types, such as HPV6, that are infrequently assocd. with cervical carcinoma lack the slice site and encode only a full-length **E6**. The authors found that, in addn. to cooperating with **E7** to immortalize keratinocytes, HPV16 **E6** can **induce** anchorage-independent growth in NIH-3T3 cells and trans-activate the **adenovirus E2 promoter**. HPV6 **E6** was also able to trans-activate the **adenovirus E2 promoter**, although it was inactive in both cell transformation assays. An HPV16 splice site mutant which expressed only the full-length HPV16 **E6** was active in all three assays, indicating that the truncated **E6** proteins are not required for these activities. The **plasmid** which encodes the truncated **E6** proteins was inactive and did not potentiate the activity of the HPV16 splice site mutant. The mutation that prevented splicing in **E6**-**E7** mRNA severely reduced the level of **E7** protein and increased **E6** protein. Taken together, the results suggest that the primary function of the splice within **E6** is to facilitate the translation of **E7** and reduce translation of full-length **E6**, rather than to generate biol. active truncated **E6** proteins.

L16 ANSWER 50 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:102486 CAPLUS
DN 116:102486
TI The **E7** functions of human papillomaviruses in rat 3Y1 cells
AU Watanabe, Sumie; Sato, Hironori; Komiyama, Naoki; Kanda, Tadahito; Yoshiike, Kunito
CS Dep. Enteroviruses, Natl. Inst. Health, Tokyo, 141, Japan
SO Virology (1992), 187(1), 107-14
CODEN: VIRLAX; ISSN: 0042-6822
DT Journal
LA English
AB Among more than 60 human papillomavirus (HPV) genotypes, several HPVs are believed to be high risk because they are found in close assocn. with cervical carcinoma. A comparison was made of the **E7** genes from HPVs 1, 6b, 16, 18, and 33 for their transactivating, transforming, and mitogenic functions in a single cell line rat 3Y1. Whereas both the low-risk (1 and 6b) and the high-risk (16, 18, and 33) HPV were transactivating for the **adenovirus E2 promoter**, only the high-risk HPVs were capable of focal transformation as assayed by an efficient method using the SR.alpha.-**promoter** and in conjunction with the HPV 16 **E6** gene. The putative oncogenicity of HPVs appears to be reflected in vitro by the focal transformation, but not by the transactivation. Transient expression of the **E7** genes controlled by the dexamethasone-responsive MMTV-LTR showed that the HPV 16 mutant E7s only with residual transforming activity were not mitogenic, but that, although the low-risk HPV E7s were less efficient, both the low-risk and high-risk HPV E7s were capable of **inducing** cellular DNA synthesis. The capability to **induce** cell DNA synthesis apparently is necessary but not sufficient for the **E7** -mediated focal transformation.

L16 ANSWER 48 OF 85 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:52855 CAPLUS
DN 116:52855
TI Transcriptional activation of several heterologous promoters by the **E6** protein of human papillomavirus type 16
AU Desaintes, Christian; Hallez, Sophie; Van Alphen, Patrick; Burny, Arsene
CS Fac. Sci., Univ. Libre Bruxelles, St. Genesius-Rode, 1640, Belg.
SO Journal of Virology (1992), 66(1), 325-33
CODEN: JOVIAM; ISSN: 0022-538X
DT Journal
LA English
AB The **E6** protein of human papillomavirus type 16 (HPV-16), along with **E7**, is responsible for the HPV-**induced** malignant transformation of the cervix. However, the mechanism of this transformation activity is not well understood. Whether the entire **E6** expression **vector** together with the reported chloramphenicol acetyltransferase (CAT) gene linked to various minimal promoters indicated that **E6** could activate transcription from a series of viral TATA-contg. promoters was investigated. Mutations or deletions that affected all upstream regulatory elements present in the thymidine kinase (TK) **promoter**, such as the GC and CAAT boxes, reduced the level of **E6**-**induced** transcription. However, compared with the basal level, these truncated promoters were still **activated** by **E6**. Although site-directed mutations of the TATA sequence present in the TK or human immunodeficiency virus long terminal repeat promoters reduced the level of basal transcription, they did not abolish the **E6**-mediated activation. Moreover, **E6** could restore almost completely the full level of wild-type **E6**-**induced** transcription as long as the upstream regulatory elements (GC/CAAT in the TK **promoter**, NF-.kappa.B in the human immunodeficiency virus long terminal repate) were intact. This dual interaction of HPV-16 **E6** is reminiscent of the activity of a coactivator.

L16 ANSWER 25 OF 85 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 97168798 EMBASE
DN 1997168798
TI HPV16 **E6** oncoprotein stimulates the transforming growth factor-.beta.1 **promoter** in fibroblasts through a specific GC-rich sequence.
AU Dey A.; Atcha I.A.; Bagchi S.
CS S. Bagchi, Ctr. Mol. Biology of Oral Diseases, College of Dentistry, University of Illinois, 801 South Paulina Street, Chicago, IL 60612, United States
SO Virology, (1997) 228/2 (190-199).
Refs: 44
ISSN: 0042-6822 CODEN: VIRLAX
CY United States
DT Journal; Article
FS 004 Microbiology
LA English
SL English
AB Human papillomaviruses (HPV) have been etiologically linked to human cervical cancer. Transforming growth factor-.beta.1 (TGF-.beta.1) is a cytokine which is a potent growth inhibitor of most epithelial, endothelial, lymphoid, and myeloid cells, but is mitogenic for mesenchymal cells and bone cells. In this study, we analyzed the effects of HPV 16 oncoproteins **E6** and **E7** on the TGF-.beta.1 **promoter**. The results showed that the HPV 16 **E6** significantly **induced** (sixfold) the TGF-.beta.1 **promoter** activity while HPV 16 **E7** showed no significant effect. The **E6** effect was cell type-specific and was observed only in the fibroblast cell lines, not in epithelial cells. **Promoter** analysis revealed that a 9-bp sequence, GGGGCGGGG, representing the consensus Sp1-binding site between -109 and -100 of the TGF-.beta.1 **promoter**, was the major target for **E6**-mediated transactivation. Mutation analysis of the **E6** polypeptide showed that the retention of amino acids between 123 and 136 of the HPV 16 **E6** protein was critical for the transactivation of the TGF-.beta.1 **promoter**. Previous studies have shown that the **adenovirus** 12S E1A oncoprotein represses the TGF-.beta.1 **promoter** by targeting an adjacent (-90 to -81) but different GC-rich sequence (TGGGTGGGG). These studies provide evidence that variant GC-rich **promoter** elements are not functionally identical and are differentially regulated by the DNA virus oncoproteins.

L16 ANSWER 17 OF 85 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

AN 1999062655 EMBASE

TI The bovine papillomavirus type 1 **E6** oncoprotein sensitizes cells to tumor necrosis factor alpha-**induced** apoptosis.

AU Rapp L.; Liu Y.; Hong Y.; Androphy E.J.; Chen J.J.

CS J.J. Chen, Department of Dermatology, New England Medical Center, 750 Washington Street, Boston, MA 02111, United States

SO Oncogene, (21 Jan 1999) 18/3 (607-615).
Refs: 70
ISSN: 0950-9232 CODEN: ONCNES

CY United Kingdom

DT Journal; Article

FS 004 Microbiology
016 Cancer
029 Clinical Biochemistry

LA English

SL English

AB Expression of viral proteins may result in susceptibility of cells to the cytotoxic effect of Tumor Necrosis Factor Alpha (TNF). While murine C127 cells containing the bovine papillomavirus type 1 (BPV-1) genome were reported to exhibit increased TNF sensitivity, the gene(s) responsible was not identified. The BPV-1 **E6** oncoprotein **induces** tumorigenic transformation of murine C127 cells and stimulates transcription when targeted to a **promoter**. BPV-1 **E6** was introduced into C127 cells (PBE6) by **retroviral** infection and stable clones were isolated. These cells showed increased apoptosis in response to TNF, as measured by several criteria. TNF-**induced** apoptosis in PBE6 cells was accompanied by increased release of arachidonic acid, indicating that phospholipase A2 was **activated** . We also provide evidence that BPV-1 **E6** mediated-sensitization of cells to TNF-**induced** apoptosis can ocur in the absence of p53.

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L7	L6 same l5	14	L7
L6	adenovir$	28488	L6
L5	l1 with l2 with l3	156	L5
L4	L3 and l2 and l1	807	L4
L3	EBNA1 or EBNA 1 or EBNA2 or EBNA 2 or EBNA-1 or EBNA-2	923	L3
L2	enhan$ or induc$ or activated	2734530	L2
L1	promoter or enhancer	159227	L1

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L7: Entry 2 of 14 File: PGPB Mar 27, 2003

DOCUMENT-IDENTIFIER: US 20030060616 A1
TITLE: Type II IL-1 receptors

Detail Description Paragraph:
[0089] B. Construction and Screening of CB23 cDNA library. A CB23 library was constructed and screened by direct expression of pooled cDNA clones in the monkey kidney cell line CV-1/EBNA-1 (which was derived by transfection of the CV-1 cell line with the gene encoding EBNA-1, as described below) using a mammalian expression vector (pDC406) that includes regulatory sequences from SV40, human immunodeficiency virus (HIV), and Epstein-Barr virus (EBV). The CV-1/EBNA-1 cell line constitutively expresses EBV nuclear antigen-1 driven from the human cytomegalovirus (CMV) immediate-early enhancer/promoter and therefore allows the episomal replication of expression vectors such as pDC406 that contain the EBV origin of replication. The expression vector used was pDC406, a derivative of HAV-EO, described by Dower et al., J. Immunol. 142:4314, 1989), which is in turn a derivative of pDC201 and allows high level expression in the CV-1/EBNA-1 cell line. pDC406 differs from HAV-EO (Dower et al., supra) by the deletion of the intron present in the adenovirus 2 tripartite leader sequence in HAV-EO (see description of pDC303 below).

Detail Description Paragraph:
[0092] The pooled DNA was then used to transfect a sub-confluent layer of monkey CV-1/EBNA-1 cells using DEAE-dextran followed by chloroquine treatment, similar to that described by Luthman et al., Nucl. Acids Res. 11:1295 (1983) and McCutchan et al., J. Natl. Cancer Inst. 41:351 (1986). CV-1/EBNA-1 cells were derived as follows. The CV-1/EBNA-1 cell line constitutively expresses EBV nuclear antigen-1 driven from the CMV immediate-early enhancer/promoter. The African Green Monkey kidney cell line, CV-1 (ATCC CCL 70, was cotransfected with 5 .mu.g of pSV2gpt (Mulligan & Berg, Proc. Natl. Acad. Sci. USA 78:2072, 1981) and 25 ug of pDC303/EBNA-1 using a calcium phosphate coprecipitation technique (Ausubel et al., eds., Current Protocols in Molecular Biology, Wiley, N.Y. 1987). pDC303/EBNA-1 was constructed from pDC302 (Mosley et al., Cell 59:335, 1989) in two steps. First, the intron present in the adenovirus tripartite leader sequence was deleted by replacing a PvuII to ScaI fragment spanning the intron with the following synthetic oligonucleotide pair to create plasmid pDC303:

First Hit Fwd Refs

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L7: Entry 7 of 14 File: USPT Nov 17, 1998

US-PAT-NO: 5837531
DOCUMENT-IDENTIFIER: US 5837531 A

TITLE: Recombinant adenoviruses for gene therapy in cancers

DATE-ISSUED: November 17, 1998

US-CL-CURRENT: 435/320.1; 424/93.2, 435/325, 435/69.1, 435/91.4, 514/44

APPL-NO: 08/ 646246 [PALM]
DATE FILED: May 13, 1996

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
FR	93 13766	November 18, 1993

PCT-DATA:

APPL-NO	DATE-FILED	PUB-NO	PUB-DATE	371-DATE	102(E)-DATE
PCT/FR94/01284	November 7, 1994	WO95/14101	May 26, 1995	May 13, 1996	May 13, 1996